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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,008	04/20/2001	Ronald M. Evans	SALK2270-4 (088802-5211)	3075

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	21

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/840,008	EVANS, RONALD M.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *3,8,13,18,23 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-7, 9-12, 14-17, 19-21, 25, 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application filed April 20, 2001 is a continuation in part of 09/458,366, filed December 9, 1999, which is a continuation in part of 09/227,718, filed January 8, 1999, which is a continuation in part of 09/005,286, filed January 9, 1998.

Applicants amendment filed June 30, 2003, paper number 18, has been received and entered. The specification has been amended. Claims 1-26 are pending.

Election/Restriction

Applicant's election with traverse of Group I, claims 1, 2, 4, 5, 6, 7, 9-12, 14-17, 19-21, 24 and 25, in Paper No. 13 is acknowledged. The traversal is on the ground(s) that separate and distinct searches would not be required. Applicants note the requirements for a proper restriction (page 1) and outlline the similarities of the inventions, and argue that the two inventions share a common core structure. Further, Applicants note that many of the claims are generic to both inventions and both groups have the same classification. This is not found persuasive because SXR and PXR are not the same molecule each having different structures at the amino acid and nucleic acid level isolated from two different mammals and each have different characteristic properties unique to themselves. Examiner acknowledges that the inventions have the same claissification, however in this case the class/subclass search is not indicative of the text and sequence search required for both inventions. Further, Examiner acknowledges that several

claims are generic to both inventions, however this is due to the nature of how the invention was claimed through the use of linking claim practice. This does not support that each of the specific molecules are the same. Finally, with respect to relationship of SXR and PXR, Examiner's interpretation that the molecules are different and unique is supported by the instant specification for example bridging pages 10-11. The specification teaches that the molecules while homologues are not structurally the same (75% similarity) nor do they share the same activation activity by various drugs ("Comparison of SXR with PXR reveals marked difference in their activation by certain drugs"- bottom of page 10). Applicants arguments are not persuasive because SXR and PXR are different and unique molecules requiring separate searches and unique consideration in the context of the claimed invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-26 are pending. Claims 3, 8, 13, 18, 23 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13. Claims 1, 2, 4, 5, 6, 7, 9-12, 14-17, 19-22, 24 and 25, as they are drawn to an expression system comprising a SXR response element and a nuclear receptor wherein the nuclear receptor is a steroid xenobiotic receptor (SXR), and methods of use for the production of a target protein in a cell, are currently under examination.

As noted in the restriction requirement, upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Specification

Applicants response filed June 30, 2003, paper number 16, (sequence listing entered as paper number 17) to the sequence requirement has been entered. The correction to the sequence listing, in particular specific base pair changes to sequences previously disclosed are noted. Upon review of the new sequence listing and the information provided in the declaration of Dr. Evans and Dr. Blumberg (filed as an attachment to paper number 18) the amendments are found to be acceptable.

However, while a sequence listing has been provided and entered, a review of the specification indicates sequences which have not been properly identified. For example at page

63, paragraph 156 the specification contains sequence listings not identified by SEQ ID NOs. The nucleotide sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

Appropriate correction is required.

For a complete response to this office action, applicant must submit the required material for sequence compliance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 5, 6, 7, 9-12, 14-17, 19-22, 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims currently under examination are drawn to an expression system comprising a SXR response element and a nuclear receptor wherein the nuclear receptor is a steroid xenobiotic receptor (SXR), and methods of use for the production of a target protein in a cell. The basis of the rejection focuses on the term SXR and in particular a steroid xenobiotic receptor as encompassed by the claims. As reviewed in Evans, steroid receptors are part of a large superfamily of receptors which are activated by the binding of a steroid or in some case xenobiotic agents wherein the binding results in binding of promoter elements and activation of gene transcription (page 891; figure 2). The complex physiology of these molecules is reviewed by Beato *et al.* who conclude that 'recent developments shows that the controls of gene expression by steroid hormones is far more complex that was apparent at the time when the genes for SHRs were isolated. With more and more players getting on stage, we realize not only this complexity but also the persuasive role steroid hormones play in a vast number of physiological and pathological precesses' (pages 855-6; bridging paragraph). Manglelsdorf *et al.* described the nuclear superfamily as over 150 different proteins with a complex array of extracellular signals and transcriptional responses (page 841; first paragraph). While the review means to stress the commonalities among various signaling pathways and that 'it is possible to consider each receptor or each hormone in isolation and to extract common themes, body physiology is rarely so simple' (page 847; bottom of column 2) and concludes that while 'the advances of the last 10 years can be viewed with satisfaction, there is still a long and challenging journey ahead' (page 484; final line). Essentially, at the time of filing of the present application,

SXR as a member of RXRs represented a growing number of superfamily members with increasingly more complex function, particularly when extended to *in vivo* physiology.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. The specification does not specifically define the term SXR but provides characteristics of a novel clone which has been isolated (page 9, paragraph 18 and figure 1A). The specification teaches that the isolated molecule encodes a protein that shares homology to other known proteins (orphan receptor proteins-page 2), however the function of each of these proteins would be considered unique and not encompassed by the activities set forth by specification for SXR (see Figure 1B and support in specification for activities of other proteins). For example, the specification identifies other related orphan nuclear receptors but specifically teaches that each has the potential to regulate a distinct endocrine signaling pathway. Beyond a simple per cent homology comparison of the orphan receptors, the specification fails to provide any specific information of how the similarities or differences between the sequences give rise to each of the unique functions. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and

which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, Applicants have cloned and defined one unique nucleic acid sequence (SEQ ID NO: 1) which encodes a SXR protein with properties that are unique from other proteins sharing sequence homology. The specification teaches how the activity of this protein was determined and how it differs from those previously disclosed in the art and that disclosed as PXR in the instant specification, however the specification fails describe the relevant identifying characteristics of the nucleic acid sequence or the protein encode thereby which provides the inherent properties of an SXR protein. The specification fails to provide a nexus between the single species of SXR isolated from nature to any other sequence which may exist or which can be derived from SEQ ID NO: 1 and still be considered a SXR protein. Further, the specification fails to completely define the nucleic acid sequences to which an SXR can bind. The skilled artisan cannot envision all the possible nucleic acid sequences encode a SXR protein or sequences to which it binds, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description *requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it* (emphasis added, see *Fiers v. Revel*, 25 USPQ2d

1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991)).

Applicants attention is drawn to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein it was stated:

In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers,* 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. *See In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Because Applicants have failed to provide an adequate written description of the materials used in the compositions and methods claimed and because there is no evidence that Applicants possessed any SXR beyond SEQ ID NO: 1 as disclosed in the instant specification, the rejected claims fail to meet the written description requirement under 35 U.S.C. 112, first paragraph. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d

1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In this case the specification only provides the required description of a SXR as set forth in SEQ ID NO: 1.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4, 5, 6, 7, 9-12, 14-17, 19-22, 24 and 25 are provisionally rejected under the judicially created doctrine of double patenting over claims 60-67, 70, 71 and 72 of copending Application No. 09/005,286. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter. In the instant case, claims 60-67, 70, 71 and 72 of 09/005,286 set forth expression vectors with regulatory elements and sequences that encode a SXR receptor protein. Further, the claims set forth that the protein is expressed in an animal cell and in claims on which they are dependent clearly set forth the specific binding site for the SXR protein being produced. The specification teaches that such expression vectors are useful in the context of expression systems as instantly claimed. Moreover, the use of the expression vectors in methods of expressing a protein of interest, either endogenous or heterologous, would be considered primary and an obvious method for using such vectors.

Conclusion

No claim is allowed. Additionally, because no linking claim has been found allowable, accordingly the invention encompassed by group II has not been examined. Again it is noted that upon the allowance of the linking claim(s), the restriction requirement as to the linked

inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

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